# **AMENDMENTS TO THE CLAIMS**

A marked-up version of the claims that will be pending following entry of the present amendments showing the amendments made herein follows. Matter that has been deleted from the claims is indicated by strikethrough or double brackets, and matter that has been added is indicated by underlining.

1. (Previously Presented) A method of tracking spread of infectious bacteria, comprising:

obtaining a plurality of bacterium samples from a plurality of patients or objects at a plurality of different physical locations;

sequencing a first region of deoxyribonucleic acid from each bacterium sample, the first region comprising consisting essentially of a variable number of tandem repeats (VNTRs) region;

storing in a database for each of the plurality of bacterium samples: a) the sequence data from the first sequenced region of each bacterium sample, and b) a physical location of the patient or object from which each bacterium sample was obtained;

comparing the sequence data stored in the database of at least two of the plurality of samples on both a base pair level and a repeat motif level;

determining a measure of phylogenetic relatedness between the compared samples based upon differences between the compared sequence data;

identifying patients infected or objects contaminated with phylogenetically related bacteria based on the phylogenetic relatedness determination;

tracking the spread over time of the bacteria based on: a) the identified patients or contaminated objects, and b) the physical locations of the identified patients or objects stored in

Barry N. KREISWIRTH *et al.* Application No.: 09/656,084

the database; and

providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the warning to control the further spread of the bacteria.

- 2. (Canceled)
- 3. (Previously Presented) The method of claim 1, wherein the database is a centralized database located remote from where the sample is obtained.
- 4. (Previously Presented) The method of claim 1, wherein the database is located in the same location as where the sample is obtained.
- 5. (Previously Presented) The method of claim 1, wherein the first region that is sequenced is a region having a mutation rate sufficient to differentiate between subspecies to determine phylogenetic relatedness and to track the bacteria.
  - 6. (Canceled)
- 7. (Previously Presented) The method of claim 6, wherein the bacterium is Staphylococcus aureus and the first region is located in the protein A gene or the coagulase gene.
- 8. (Previously Presented) The method of claim 7, wherein each bacterium sample is obtained from a patient as the patient is admitted to a health care facility and prior to being

exposed to patients in the health care facility.

## 9. (Canceled)

10. (Previously Presented) The method of claim 1, further including:obtaining a medical history from a patient from which at least one of the plurality of

bacterium samples was taken;

determining an infection risk factor based on the patient's medical history, the infection risk factor being a measure of the patient's risk of acquiring an infection; and taking appropriate infection control measures in accordance with the infection risk factor.

11. (Previously Presented) The method of claim 10, further including:

transmitting the patient's medical history to the database without transmitting private patient information; and

storing the private patient information in a local database at the remote from the database that the patient's medical history is transmitted to.

- 12. (Previously Presented) The method of claim 1, wherein the step of sequencing comprises either:
- a) sequencing the first region at a remote facility and transmitting the resulting sequence data to the database via a computer network; or
- b) sending each of the plurality of bacterium samples to an infection control facility associated with the database, sequencing the first region at the infection control facility, and

Barry N. KREISWIRTH et al. Application No.: 09/656,084

storing the sequence data in the database.

13. (Original) The method of claim 1, wherein the first region is identified by a set of primers.

14. (Original) The method of claim 1, wherein the first region is amplified prior to sequencing.

15. (Canceled)

16. (Previously Presented) The method of claim 1, wherein the step of determining the phylogenetic relatedness between the compared samples includes:

identifying repeat sequences in the sequence data for each of the compared samples; and treating the insertion or deletion of a repeat sequence as a single genetic event.

17. (Previously Presented) The method of claim 16, wherein determining the phylogenetic relatedness between the compared samples further including:

treating an insertion or deletion of an individual nucleotide as a single genetic event.

18. (Canceled)

19. (Canceled)

Barry N. KREISWIRTH *et al.* Application No.: 09/656,084

## 20. (Canceled)

21. (Previously Presented) The method of claim 1, wherein the step of determining the phylogenetic relatedness between the compared samples includes at least one of:

comparing a first bacterium sample to other samples obtained from the same facility as where the first bacterium sample was taken, thereby determining a local phylogenetic relatedness;

comparing the first bacterium sample other samples obtained from the same geographical region as where the first bacterium sample was taken, thereby determining a regional phylogenetic relatedness; and

comparing the first bacterium sample other samples obtained globally, thereby determining a global phylogenetic relatedness.

22. (Previously Presented) The method of claim 1, wherein the steps of storing in a database and tracking the spread of the infection further comprises:

transmitting over a computer network from a remote facility to an infection control server the sequence data from the first sequenced region of each of the plurality of bacterium samples and the physical location of the patient or object from which each bacterium sample is taken.

23. (Previously Presented) The method of claim 22, further including:

storing a map of the physical location of where the plurality of samples were obtained in the database; and

determining the spread of the infection based on the map.

- 24. (Previously Presented) The method of claim 23, further including: sensing the patient's physical location prior to transmitting the patient's physical location.
- 25. (Previously Presented) The method of claim 1, further including:

determining the virulence of the bacterium by retrieving the virulence data of identical or similar bacteria from the database; and

transmitting over a computer network virulence information to a location where the bacterium sample was obtained.

26. (Previously Presented) The method of claim 1, further comprising:

determining drug resistance and treatment information of the bacterium by retrieving drug information data of identical or similar bacteria from the database; and

transmitting over a computer network the drug information data to a location where the bacterium sample was obtained.

27. (Previously Presented) The method of claim 1, wherein providing a warning includes:

determining whether a location where each bacterium was obtained has an outbreak problem; and

transmitting over a computer network an outbreak warning to each location having an outbreak problem.

28. (Previously Presented) The method of claim 1, further including:
sequencing a second region of the nucleic acid of each bacterium sample;
storing the sequence data from the second region of the nucleic acid of each bacterium sample in a database;

comparing the second sequenced region of at least two of the plurality of samples, wherein the determining a measure of phylogenetic relatedness comprises; and

determining a measure of phylogenetic relatedness based on the comparison of the first and second sequenced regions.

- 29. (Original) The method of claim 28, wherein the determination of relatedness based on the second sequenced region is used to verify the determination of relatedness based on the first sequenced region.
- 30. (Previously Presented) The method of claim 28, further including: identifying a first level of subspecies of each bacterium sample based on the first sequenced region; and

identifying a second level of subspecies of each bacterium sample based on the second sequenced region.

31. (Original) The method of claim 28, further including:

tracking the global spread of an infection based on sequencing and comparing a slowly mutating region of the nucleic acid; and

tracking the local spread of an infection based on sequencing and comparing a more

rapidly mutating region of the nucleic acid.

32. (Currently amended) A system for tracking spread of infectious bacteria, comprising:

a computer network;

a centralized database;

a remote facility connected to the computer network, the remote facility obtaining a plurality of bacterium samples from a plurality of patients or objects at a plurality of different locations;

a server connected to the computer network, the server receiving sequence data for a first sequenced region of a nucleic acid from each of the plurality of bacterium samples and a physical location of a patient or object from which each bacterium sample was obtained, the first sequenced region comprising consisting essentially of a variable number of tandem repeats (VNTRs) region;

storing in a database for each of the plurality of bacterium samples: a) the sequence data from each of the plurality of bacterium samples, and b) the physical location of the patient or object from which each bacterium sample was obtained;

accessing the centralized database and comparing the stored sequence data of at least two of the plurality of bacterium samples on both a base pair level and a repeat motif level;

determining a measure of phylogenetic relatedness between the compared samples;

identifying patients infected or objects contaminated with phylogenetically related bacteria based on the phylogenetic relatedness determination;

tracking the spread over time of the bacteria based on a) the identified patients or objects,

and b) and the physical locations of the identified patients or objects stored in the database; and transmitting a warning over the computer network to the remote facility based on the tracking of the spread of the bacteria, thereby allowing the remote facility to control the further spread of the bacterial infection.

33. (Currently amended) Computer executable software code stored on a computer readable medium, for performing a method of tracking spread of infectious bacteria over a computer network, comprising:

obtaining a plurality of bacterium samples from a plurality of patients at a plurality of different locations;

sequencing a first region of a nucleic acid from each of the pluralility of bacterium samples, the first region comprising consisting essentially of a variable number of tandem repeats (VNTRs) region;

storing in a database: a) the sequence data from the first sequenced region of each bacterium sample, and b) a physical location of a patient or object from which each bacterium sample was obtained;

comparing the stored sequence data of at least two of the plurality of samples on both a base pair level and a repeat motif level;

determining a measure of phylogenetic relatedness between the compared samples; identifying patients infected or objects contaminated with phylogenetically related bacteria based on the phylogenetic relatedness determination;

tracking the spread of the bacteria based on the identified patients or objects and the physical locations of the identified patients and objects stored in the database; and

providing bacterial spread information based on the tracking of the spread of the bacteria, thereby allowing use of the bacterial spread information to further control the spread of the bacteria.

- 34. (Previously Presented) The method of claim 1, wherein the plurality of bacterium samples are obtained at a facility remote from where the sequencing is carried out.
- 35. (Previously Presented) The method of claim 34, wherein the remote facility is a health care facility, and the sample of the bacterium is obtained from a patient as the patient is admitted to a health care facility and prior to being exposed to patients in the health care facility.
- 36. (Previously Presented) The method of claim 1, wherein the sample is obtained at a facility remote from where the sequencing, comparing and determination of a measure of phylogenetic relatedness are carried out.

#### 37. (Canceled)

- 38. (Previously Presented) The method according to claim 1, wherein infected patients are identified prior to an outbreak of the bacterial infection.
  - 39. (Canceled)
  - 40. (Canceled)

### 41. (Canceled)

42. (Withdrawn) A method of tracking the spread of bacteria, comprising: obtaining a plurality of bacterium samples from a plurality of patients at a plurality of different locations;

sequencing a first region of deoxyribonucleic acid from each of the plurality of bacterium samples, the first region comprising consisting essentially of a variable number of tandem repeats (VNTRs) region;

storing in a database: a) the sequenced data from each bacterium sample; and b) the location of the each patient;

comparing the stored sequence data of at least two of the plurality of bacterium samples on both a base pair level and a repeat motif level;

determining the phylogenetic relatedness of the sequence data between the compared samples based on: a) the number of insertions and deletions of individual nucleotides; and b) the number of insertions and deletions of repeat cassettes, wherein a repeat cassette comprises a sequence of nucleotides which repeats in the first region of the deoxyribonucleic acid;

tracking the spread over time of the bacteria based on a) the phylogenetic relatedness determination, and b) the physical locations of the patients stored in the database; and providing a warning based on the tracking of the spread of the bacteria wherein the warning allows the recipient of the warning to control the further spread of the bacteria.

43. (Withdrawn) A method of tracking the spread of bacteria, comprising:

obtaining a plurality of bacterium samples from a plurality of patients at a plurality of different locations;

sequencing a first region of deoxyribonucleic acid from each of the plurality of bacterium samples, the first region emprising consisting essentially of a variable number of tandem repeats (VNTRs) region;

storing in a database: a) the sequenced data from each bacterium sample; and b) the location of the each patient;

comparing the stored sequence data of at least two of the plurality of bacterium samples on both a base pair level and a repeat motif level;

determining the phylogenetic relatedness of the sequence data between the compared samples, wherein the insertion or deletion of a repeat cassette is treated as a single genetic event, wherein a repeat cassette comprises a sequence of nucleotides which repeats in the first region;

tracking the spread over time of the bacteria based on a) the phylogenetic relatedness determination, and b) the physical locations of the patients stored in the database; and providing a warning based on the tracking of the spread of the bacteria wherein the

warning allows the recipient of the warning to control the further spread of the bacteria.

# 44. (Previously Presented)The system of claim 32, further comprising:

sequencing the first region of the nucleic acid for each of the plurality of bacterium samples at the remote facility; and

transmitting the sequence data to the server over a computer network.